

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of

Joel R. Studin

Serial No.

10/829,315

Filed

April 21, 2004

Examiner

Sheikh, Humera N.

Art Unit

1615

Title

Method and Composition for the Treatment of Scars

Commissioner of Patents and Trademarks

P.O. Box 1450

Alexandria, VA 22313-1450

DECLARATION OF JOEL R. STUDIN UNDER 37 C.F.R. §1.132

I do hereby declare as follows:

- 1. THAT I received a Bachelor of Science in General Science and Psychology from the University of Rochester, Rochester, NY, in 1975.
- 2. THAT I received a Doctor of Medicine from Mount Sinai Hospital, New York, NY, in 1982.
- 3. THAT I have practiced as a Plastic and Reconstructive Surgeon since 1987.
- 4. THAT I am the inventor of the above-identified application, that I am familiar with the above-identified application, the Office Actions and applied references rendered to date.
- 5. Exhibit A is a testing report received from Bryce RX Laboratories, Inc., detailing the results of transdermal affect testing conducted by Bryce. I authorized Bryce RX Laboratories Inc. to undertake the transdermal affect testing. All dates and extraneous information have been redacted from Exhibit A.
- 6. Exhibit A reports the transdermal effectiveness evaluation of various possible carriers for delivering topical treatments including corticosteroids for scar tissue, psoriasis, eczema and other cutaneous maladies.

 Transdermal effectiveness was determined by the well-known McKenzie-Stoughton vasoconstriction assay. The McKenzie-Stoughton assay is a skin-blanching test. Under this assay a test sample containing a carrier and hydrocortisone was applied to a test subject's skin and the degree of skin blanching was observed. In accordance with the test, hydrocortisone

adsorbed into the skin causes a localized vasoconstriction at the site of application of the test sample. This vasoconstriction causes the skin to appear white. The more hydrocortisone that was adsorbed into the skin, the whiter the localized spot appeared. At 1, 2, and 4-hour time intervals an observer assessed the amount of skin blanching on a scale of 0 (least blanching) to 4 (most blanching). After all data had been collected from three different observers, the scores were added up to give a total blanching score. The higher the score, the higher the level of blanching, and thus, the higher the level of hydrocortisone adsorbed into the skin.

- 7. Exhibit A, page 1, provides further details for the preparation of the samples tested, and testing of those samples. Briefly, 50 ml of a carrier was added to a 200 ml beaker. 1 gm of hydrocortisone was added to the beaker and mixed until fully dissolved. Water was then added to a final volume of 100 ml. According to page 1, a 0.3 cc aliquot of each mixture was placed onto a subjects forearm and marked with a sharpie. Blanching was then observed at 1, 2, and 4-hour time intervals, and vasoconstriction was assessed on a scale of 0 (least blanching) to 4 (most blanching).
- 8. Exhibit A, pages 2-5, provides the blanching results from three observers at 1, 2, and 4-hour time intervals on four different test subjects for each carrier tested. Page 6 provides the cumulative score for each carrier tested for all four test subjects. As can be seen from page 6, Nitrocellulose (Flexible Collodion) had the highest test score (141), which indicates the greatest degree of blanching, and thus, the highest degree of transdermal transmission of the active agent (hydrocortisone) tested.
- 9. Exhibit A, page 6, also provides blanching results for methyl cellulose (14), hydroxymethylcellulose (25), nitrocellulose (flexible collodion/xanthan gum) (59), hydroxyethylcellulose (29), cellulose acetate (23), propylene glycol (7), aluminum hydroxide (49) and tragacanth (3). As can be clearly see from these results nitrocellulose showed very strong transmission of the active agent (hydrocortisone) into the test subject's skin.



Bryce RX Laboratories, INC. DEA BB5460706

*** TESTING REPORT *** PAGE 1

Formula: Scar/Ecz/Psoriasis

Client: Dr. Joel Studin

TRANSDERMAL AFFECT TESTING SCAR/ECZ/PSORIASIS - DR. STUDIN

The goal of this testing is to ascertain the relative efficacy of a number of possible carriers for delivering topical treatments including corticosteroids for scar tissue, psoriasis, eczema and other cutaneous maladies.

- METHOD / PROCESS- -

Transdermal effectiveness evaluation to be performed using the Coleman, Kanfer and Haigh method of the McKenzie - Stoughton vasoconstriction assay.

- 1. Place 50 ml of carrier into a swoml beaker
- 2. Place igm hydrocortisone into beaker
- 3. Mix until fully dissolved or evenly dispersed
- 4. Q5 to 100ml
- 5. Seal beaker with plastic wrap
- 6. Repeat for all carriers.
- 7. Place 0.3cc aliquot of each mixture on flexor surface of subject forearm and mark with Sharpie
- 8. Subject to wear short sleeves and avoid washing or sweating
- 9. Observe at 1,2 and 4 hours
- io. Chart observation of skin blanching by subject and z observers
- 11. Vasoconstriction assessed on a scale of zero=least blanching to 4=most blanching

**** THIS TESTING IS A TRADE SECRET OF BRYCE RX LABORATORIES, INC. ****

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Observation 1	zhr_		zhr_	ନ	4har_	0	
Observation 2	ahr	1.	shr	0	abr.	C)	
Subject #1	a.tix_	Ō	ahr_	<u>چ</u>	4hr	Ç)	Total Score <u> 2</u>
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Observation <u>2</u> Subject #1		<u> </u>	&U);		4nr_	<u>Ei</u>	
Subject #1	INE_		2nr_		4hr_	Ø	lotal Score <u>s</u> _
Nitrocellulose (Flexible							
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Subject #1	1hr_	2	zhr_		4hr_	1	Total Score <u>14</u>
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Subject #1		2	zhr_	ø	4hr	ē	Total Scorez
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Cellulose Acetate							
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Observation <u>2</u>	thr_		spr_	0	4hr	Ø	
Subject #g	thr_	ନ	2hr_	0	4h£	B	Total Score <u>a</u>
Propylene Glycol							
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Observation <u>z</u>		a .	zhr	Ю	abr	ris .	
Subject #1	n.hr	Ø		8	4hr	ڻ ن	— Total Soore e
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Aluminum Hydroxide							
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Observation <u>a</u>	ihr_	<u> 2</u>	zhr	7.	4hr	1	
Subject #1	1hr	2	shr_	1	4hr	_1	_Total Score14
Tragacanth							
Observation 1	a.hr	а	abr	o.	aber		• '
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Subject #1		es ·	4114 	0	411£ 4h£		—- ———————————————————————————————————
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Best Available Copy

10. I further declare that all statements made herein to my knowledge are true and that all statements made on information and belief are believed to be true: and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements so made may jeopardize the validity of the document, or application, or any patent issuing therefrom.

Respectfully submitted,

3/21/08

Joel R. Studin

.Methyl Cellulose					•			
Observation 1	1hr_		zhr_		ahr	1	•	
Observation <u>z</u>	ıhr	. 2	ahx		4hr	0		
Subject #2		1	shr_	ଜ	4hr_	ø	Total Score7_	
							·	
Hydroxymethylcellulose								
Observation 1	zhr_		spr_					
Observation <u>a</u>						ø	<u> </u>	
Subject #2	thr_	1	ehr_	Ø	4hz_	ତ	Total Score <u>6</u>	
Nitrocellulose (Flexib	le Collod	ion)						
Observation 1	ihr_	ব	shr	4	ahr	4		
Observation <u>s</u>	ihr	4	2hr	d	ahr	· 4		
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Subject #2							Total Carre	
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Hydroxyethylcellulose								
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Subject #2	thr_	J	zhr_	0	4hr_	6)	Total Score <u>8</u>	
Cellulose Acetate					٠			
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Observation <u>s</u>		7		7	4 5 2°	<u> </u>		
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Propylene Glycol								
Observation 1	1hr_	1	ahr_	Ø	4hr_	B		
Observation a		11			4hr_			
Subject #2		0					Total Score <u>s</u>	_
Aluminum Hydroxide								
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Observation 2	thr_				4hr			
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Tragacanth				·			•	
Observation 1	ihr_	ø	ahr_	Ö	4hr_	œ	•	
Observation <u>z</u>	1hr	0	zhr		4hr	Ö	· ·	
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Methyl Cellulose							
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Observation <u>2</u>	ihr_	_a_	zhr_	1	4hr_		
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Subject #3			abr	- 3	4112 452	—±——	Total Šoora so
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Cellulose Acetate							
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Observation <u>p</u>					4hr		
Subject #g							 Total Score <u></u>
Propylene Glycol							·
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Aluminum Hydroxide							
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Subject #a	1hr_	_2	2hr_		4ħ£	_1	Total Score <u>11</u>
Tragacanth							
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Observation <u>z</u>	ihr_			ø			
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Methyl Cellulose							
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Observation <u>2</u>			znr_	_4_	4nr_	_4	
Subject #4	1Fi£	3		<u>a</u>	4nr_	-4	otar poorssz
Nitrocellulose (Flexible	Collod	ion /	Xanth	an Gu	am)		
Observation 1	ihr_	2	zhr_	ı	4hr_	ı	
Observation <u>a</u>	ahr_	2	zhr_	2 ·	4hr_	1	
Subject #4	ahr_	3	ahr_	_2		1.	Total Score 15
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Hydroxyethylcellulose							
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Observation <u>2</u>	1hr_	1	zhr_		4hr_	0	
Subject #4	1hr_	1	2hr_	0	4hr_	©.	Total Score_ 5
Cellulose Acetate							
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Propylene Glycol							
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BASE CARRIER CUMULATIVE TOTAL SUBJECTS 1-4 (1HR, 2HR, 4HR)

Methyl Cel	lulose	* .	
Subjects	#1-4	Total Score <u>ı</u>	ব
Hydroxymet	hylcellulose		
Subjects	#1-4	Total Score	5
Nitrocellu	lose (Flexible (Collodion)	
Subjects	#1-4	Total Scorel	43
Nitrocellu	lose (Flexible (Collodion / Xanthan	Gum 3
Subjects	#1-4	Total Score5	<u>a</u>
Hydroxyeth	ylcellulose		
Subjects	#1-4	Total Score <u>s</u>	<u>= </u>
Cellulose	Acetate		
Subjects	#1-4	Total Score 2:	3
Propylene (Glycol		
Subjects		Total Score 💯 🛪	
Aluminum Hy	vdrosi de		
Subjects		Total Score49	a
	•		
Tragacanth			
Subjects	#1-4	Total Score g	

Conclusion

Most carriers showed very poor transdermal transmission of the active. Nitrocellulose however, showed a very strong transmission in our formulation. We believe that this is a result of increased bio-electric binding. It is our suggestion that you continue the development of your products using the nitrocellulose base that you suggested.